

REMARKS

Claims 1-28 have been cancelled, and new claims 29-59 have been added.

Attached is a version with markings to show changes made to the first paragraph of the specification, marked up to show all the changes relative to the previous version of the paragraph, pursuant to 37 C.F.R. §1.121(b)(iii).

I. Amendments

New claims 29-59 find basis in the specification of the priority application no. 60/028,269 filed October 11, 1996, as follows:

New Claim Number	Support for new claim
29	<p><i>"A method of administering a therapeutic agent, comprising, administering via inhalation"; page 32, line 21; "liposomes formed of vesicle-forming lipids"; page 9, line 4 "and having a coating of hydrophilic polymer chains on the liposome outer surface,"; page 9, lines 9-10; "said liposomes having an entrapped therapeutic agent"; page 4, lines 20-21.</i></p>
30	<p><i>"the vesicle-forming lipid is selected from the group consisting of hydrogenated soy phosphatidylcholine, distearoylphosphatidylcholine sphingomyelin, diacyl glycerol, phosphatidyl ethanolamine, phosphatidylglycerol, distearyl phosphatidylcholine, and distearyl phosphatidylethanolamine"; page 13, lines 3-5 and 13-15; page 14, lines 13-14.</i></p>
31	<p><i>"said liposomes further contain a shielded cationic lipid effective to impart a positive liposome-surface charge"; page 6, lines 6-8.</i></p>
32	<p><i>"the cationic lipid is selected from the group consisting of 1,2-dioleyloxy-3-(trimethylamino)propane, N-[1-(2,3,3-ditetradeeyloxy)propyl]-N,N-dimethyl-N-hydroxyethylammonium bromide, N-[1-(2,3,3-dioleyloxy)propyl]-N,N-dimethyl-N-hydroxy ethylammonium bromide, N-[1-(2,3-dioleyloxy) propyl]-N,N,N-trimethylammonium chloride; 3β[N-(N',N'-dimethylaminoethane)</i></p>

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	<i>carbamoly] cholesterol; and dimethyldioctadecylammonium"; page 14, lines 23-31.</i>
33	<i>"the cationic lipid is a neutral lipid derivatized with a cationic lipid"; page 14, lines 32-35.</i>
34	<i>"said hydrophilic polymer coating is composed of hydrophilic polymers selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropylmethacrylamide, polymethacrylamide, polydimethylacrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethyleneglycol, and polyaspartamide"; page 4, line 35 through page 5, line 8.</i>
35	<i>"said hydrophilic polymer coating is composed of polyethylene glycol chains"; page 15, lines 22-23; "having a molecular weight of between about 500 Daltons and about 10,000 Daltons"; page 5, lines 8-10.</i>
36	<i>"between about 1 mole percent and about 20 mole percent of the vesicle-forming lipids are derivatized with said hydrophilic polymer chains"; page 10, lines 25-28.</i>
37	<i>"at least a portion of the hydrophilic polymers are joined by a chemically releasable bond"; page 6, lines 28-30.</i>
38	<i>"said releasable bond is a disulfide bond"; page 18, line 29.</i>
39	<i>"said releasable bond is a pH</i>

	<i>sensitive chemical linkage"; page 6, lines 33-35.</i>
40	<p><i>"the liposomes are composed of between about 70-90 mole percent hydrogenated soy phosphatidylcholine"; page 13, lines 1-3 and page 29, lines 29-32;</i></p> <p><i>"about 1-20 mole percent distearylphosphatidylcholine derivatized with polyethyleneglycol"; page 14, lines 12-14 and page 10, lines 25-28;</i></p> <p><i>"and about 1-50 mole percent cholesterol"; page 30, lines 19-20.</i></p>
41	<i>"the liposome is about 0.1 to about 10 microns"; page 29, lines 27-28.</i>
42	<i>"the agent entrapped in the lipid vesicles is a polynucleotide capable of expressing a selected protein, when taken up by a target cell"; original claim 13.</i>
43	<i>"the agent entrapped in the liposomes is an oligonucleotide or oligonucleotide analog effective for sequence-specific binding to cellular RNA or DNA"; page 17, lines 7-10.</i>
44	<i>"the agent entrapped in the liposomes is selected from the group consisting of DNA, proteins, and peptides"; page 37, lines 11-12, page 32, line 4, page 33, line 1.</i>
45	<i>"the agent entrapped in the liposomes is selected from the group consisting of antibiotics, antivirals, and antitumor drugs"; page 5, lines 31-33; page 19, lines 20-22.</i>
46	<i>"said liposomes further contain a ligand attached to the distal end of at least a portion of said hydrophilic polymer chains"; page</i>

	5, lines 24-25.
47	"the liposomes further include a ligand attached the polar head group of at least a portion of the vesicle-forming lipids of the liposome"; page 6, lines 1-3.
48	"the ligand is an antibody or an antibody fragment"; page 21, lines 24-29.
49	"the ligand is a Fab' fragment of an antibody"; page 21, lines 24-29.
50	"the ligand is a single chain Fv antibody"; page 21, lines 24-29 describes an antibody fragment.
51	"the ligand binds to an extracellular domain of a growth factor receptor"; Table 1, pages 20-21.
52	"the receptor is selected from the group consisting of epidermal growth factor receptor, basic fibroblast growth factor receptor and vascular endothelial growth factor receptor"; page 21, lines 7-9.
53	"the ligand binds a receptor selected from the group consisting of E-selectin receptor, L-selectin receptor, P-selectin receptor, folate receptor, CD4 receptor, $\alpha\beta$ integrin receptors and chemokine receptors"; page 20, line 33 and 35; page 21, lines 5-6, 10, and 22-23.
54	"the ligand is selected from the group consisting of folic acid, pyridoxal phosphate, sialyl Lewis ^x , transferrin, epidermal growth factor, basic fibroblast growth factor, vascular endothelial growth factor, VCAM-1, ICAM-1, PECAM-1, and RGD peptides"; page 20, lines 33 and 35; page 21, lines 3, 5, 7-12, and 15-16.

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55	"the ligand is selected from the group consisting of water soluble vitamins, apolipoproteins, insulin, galactose, Mac-1, PECAM-1/CD31, fibronectin, osteopontin, RGD sequences of matrix proteins, HIV GP 120/41 domain peptomers, GP120 C4 domain peptomers, T cell tropic isolates, SDF-1 chemokines, Macrophage tropic isolates, anti-cell surface receptor antibodies or fragments thereof, pyridoxyl ligands, RGD peptide mimetics, and anti-E-selectin Fab"; page 20, line 34; page 21, line 1-2, 4, 6, 12-29.
56	"the anti-cell surface receptor antibodies or fragments thereof is selected from the group consisting of anti-selectin and anti-VEGF pyridoxyl"; page 21, lines 5-7.
57	"the pyridoxyl ligand is selected from the group consisting of pyridoxal, pyridoxine, pyridoxamine, pyridoxal 5'-phosphate and N-(4'-pyridoxyl)amines"; page 22, lines 10-12.
58	"said liposomes are further comprised of a lipid derivatized by a diblock copolymer composed of a hydrophobic polymer chain covalently bound to the lipid and a hydrophilic polymer chain, the hydrophobic and hydrophilic chains being joined by a bond effective to release the hydrophilic polymer chains in response to an existing or an induced physiologic condition, thereby exposing the hydrophobic polymer chains"; page 4, lines 28-33; page 6, line 28 through page 7, line 3.
59	"said hydrophobic polymer is

	<p><i>selected from the group consisting of polypropylene oxide, polyethylene, polypropylene, polycarbonate, polystyrene, polysulfone, polyphenylene oxide and polytetramethylene ether"; page 5, lines 11-14.</i></p>
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If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

This application is a continuation of U.S. Application No. 09/876,707 filed June 7, 2001, now pending; which is a division of U.S. Application No. 09/517,224 filed March 2, 2000, now U.S. Patent No. 6,316,024; which is a division of U.S. Application No. 09/138,480 filed August 21, 1998, now U.S. Patent No. 6,056,973; which is a continuation-in-part of U.S. Application No. 08/949,046 filed October 10, 1997, now U.S. Patent No. 5,891,468; which claims the priority of U.S. Provisional Application No. 60/028,269, filed October 11, 1996, now abandoned, which are all incorporated herein by reference in [its]their entirety.